

WHAT IS CLAIMED IS:

1. A means for propagating replication-defective adenovirus in an adenoviral E1-complementing cell line expressing E1 gene product(s) which are non-native to the adenovirus, which comprises:
 - (a) inserting all or a portion of a heterologous adenoviral E4 region comprising nucleic acid sequence encoding open reading frame 6 (ORF6) into a replication-defective adenovirus; wherein the E4 region or portion thereof inserted into the adenovirus is native to a virus of the same adenovirus serotype as the E1 gene product(s) expressed by the complementing cell line;
 - (b) introducing the replication-defective adenovirus into the adenoviral E1-complementing cell line;
 - (c) allowing the replication-defective adenovirus to propagate in the adenoviral E1-complementing cell line; and
 - (d) rescuing the propagated adenovirus.
2. A means in accordance with claim 1 wherein the heterologous adenoviral E4 region or portion thereof comprises the complete adenoviral E4-encoding region.
3. A means in accordance with claim 2 wherein the heterologous adenoviral E4 region or portion thereof comprises the complete adenoviral E4-encoding region and native E4 promoter.
4. A means in accordance with claim 1 wherein the heterologous adenoviral E4 region or portion thereof is inserted into the replication-defective virus in place of nucleic acid sequence encoding open reading frame 6 (ORF6).

5. A means in accordance with claim 1 wherein the heterologous adenoviral E4 region or portion thereof is inserted into the replication-defective virus in place of nucleic acid sequence encoding the complete adenoviral E4-encoding region.

6. A means in accordance with claim 1 wherein the heterologous adenoviral E4 region or portion thereof is derived from a subgroup C adenovirus.

7. A means in accordance with claim 1 wherein the subgroup C adenovirus is adenovirus of serotype 5.

8. A means in accordance with claim 7 wherein the replication-defective adenovirus is an adenovirus of subgroup B.

9. A means in accordance with claim 7 wherein the replication-defective adenovirus is an adenovirus of serotype 35.

10. A means in accordance with claim 1 wherein the heterologous adenoviral E4 region or portion thereof is operatively linked to a heterologous promoter.

11. A means in accordance with claim 1 wherein the adenoviral E1-complementing cell line is a PER.C6® cell line.

12. A replication-defective adenovirus comprising all or a portion of a heterologous E4 region comprising a heterologous adenoviral open reading frame 6 (ORF6).

13. A replication-defective adenovirus in accordance with claim 12 wherein the adenovirus comprises a heterologous gene of interest.

14. A replication-defective adenovirus in accordance with claim 13 wherein the heterologous gene of interest is a gene encoding an HIV-1 antigen.

15. A replication-defective adenovirus in accordance with claim 14 wherein the HIV-1 antigen is selected from the group consisting of HIV-1 gag, pol, nef and env.

16. A replication-defective adenovirus comprising all or a portion of a heterologous E4 region comprising a heterologous adenoviral open reading frame 6 (ORF6) and a gene encoding HIV-1 gag.

5 17. A replication-defective adenovirus comprising all or a portion of a heterologous E4 region comprising a heterologous adenoviral open reading frame 6 (ORF6) in place of a native E4 region or portion thereof comprising ORF6.

18. A replication-defective adenovirus comprising all or a portion of a heterologous E4 region comprising a complete heterologous E4 region in place of a complete native E4 region.

10 19. A replication-defective adenovirus comprising a heterologous E4 region or portion thereof comprising a complete heterologous E4 region including E4 promoter in place of a complete native E4 region.

20. Adenovirus propagated in accordance with the means of claim 1.

15 21. A means in accordance with claim 1 wherein the replication-defective adenovirus comprises a heterologous gene of interest.

22. A means in accordance with claim 21 wherein the heterologous gene of interest is a gene encoding an HIV-1 antigen.

23. A means in accordance with claim 22 wherein the HIV-1 antigen is selected from the group consisting of: HIV-1 gag, pol, nef and env.

20 24. A replication-defective adenovirus of serotype 35 comprising all or a portion of an adenovirus serotype 5 E4 region comprising open reading frame 6 (ORF6) and a heterologous gene of interest.

25. A replication-defective adenovirus in accordance with claim 24 wherein the heterologous gene of interest is a gene encoding an HIV-1 antigen.

26. A replication-defective adenovirus in accordance with claim 25 wherein the HIV-1 antigen is selected from the group consisting of: HIV-1 gag, pol, nef and env.
27. A replication-defective adenovirus of serotype 35 comprising all or a portion of an adenovirus serotype 5 E4 region comprising open reading frame 6 (ORF6) and a
5 gene encoding HIV-1 gag.
28. A recombinant adenoviral vector of serotype 24 which comprises an E4 gene or a segment of an E4 gene comprising open reading frame 6 ("ORF6") of an alternative serotype.
29. A population of cells comprising the recombinant adenoviral vector of
10 claim 28.
30. A method for producing recombinant, replication-defective adenovirus particles comprising:
- (a) introducing a recombinant adenoviral vector of claim 28 into a population of cells expressing adenovirus E1; and
- 15 (b) harvesting the resultant recombinant, replication-defective adenovirus.
31. Purified recombinant, replication-defective adenovirus particles harvested in accordance with the method of claim 30.
32. A composition comprising purified recombinant adenovirus particles in accordance with claim 31.
- 20 33. A composition in accordance with claim 32 which comprises a physiologically acceptable carrier.
34. A recombinant adenoviral vector in accordance with claim 28 which is at least partially deleted in E1 and devoid of E1 activity and comprises a heterologous nucleic acid.

35. A composition comprising purified recombinant adenoviral particles in accordance with claim 31 which are at least partially deleted in E1 and devoid of E1 activity and comprise a heterologous nucleic acid.

5 36. A method for effecting the delivery and expression of heterologous nucleic acid comprising administering the composition of claim 35 prior or subsequent to administration of the heterologous nucleic acid with the same or different vector.

37. A method in accordance with claim 36 wherein the composition is preceded or followed by administration of heterologous nucleic acid with an adenovirus of a different serotype.

10 38. A composition in accordance with claim 35 wherein the heterologous nucleic acid encodes an HIV antigen.

39. A method for generating a cellular-mediated immune response against HIV in an individual comprising administering to the individual a composition of claim 38.

15 40. A composition in accordance with claim 39 wherein the HIV antigen is HIV-1 gag or immunologically relevant modification thereof.

41. A composition in accordance with claim 39 wherein the HIV antigen is HIV-1 nef or immunologically relevant modification thereof.

42. A composition in accordance with claim 39 wherein the HIV antigen is HIV-1 pol or immunologically relevant modification thereof.

20 43. A recombinant adenoviral vector of serotype 24 which is at least partially deleted in E1 and devoid of E1 activity; wherein said vector comprises an E4 gene or a segment of an E4 gene from adenovirus serotype 5 comprising open reading frame 6 ("ORF6"), and a heterologous nucleic acid.

44. A population of cells comprising the recombinant adenoviral vector of claim 43.

45. A method for producing recombinant, replication-defective adenovirus particles comprising:

5 (a) introducing a recombinant adenoviral vector of claim 43 into a population of cells expressing adenovirus serotype 5 E1; and

(b) harvesting the resultant recombinant, replication-defective adenovirus.

46. Purified recombinant, replication-defective adenovirus particles harvested in accordance with the method of claim 45.

10 47. A composition comprising purified recombinant adenovirus particles in accordance with claim 46.

48. A composition in accordance with claim 47 which comprises a physiologically acceptable carrier.

15 49. A method for effecting the delivery and expression of the heterologous nucleic acid comprising administering the composition of claim 48 prior or subsequent to administration of the heterologous nucleic acid with the same or different vector.

50. A method in accordance with claim 49 above wherein the composition is preceded or followed by administration of the heterologous nucleic acid with an adenovirus of a different serotype.

20 51. A composition in accordance with claim 48 wherein the heterologous nucleic acid encodes an HIV antigen.

52. A method for generating a cellular-mediated immune response against HIV in an individual comprising administering to the individual a composition of claim 51.

53. A composition in accordance with claim 51 wherein the HIV antigen is HIV-1 gag or immunologically relevant modification thereof.

54. A composition in accordance with claim 51 wherein the HIV antigen is HIV-1 nef or immunologically relevant modification thereof.

5 55. A composition in accordance with claim 51 wherein the HIV antigen is HIV-1 pol or immunologically relevant modification thereof.

56 A recombinant adenoviral vector of serotype 34 which comprises an E4 gene or a segment of an E4 gene comprising open reading frame 6 ("ORF6") of an alternative serotype.

10 57. A population of cells comprising the recombinant adenoviral vector of claim 56.

58. A method for producing recombinant, replication-defective adenovirus particles comprising:

(a) introducing a recombinant adenoviral vector of claim 56 into a population of
15 cells expressing adenovirus E1; and

(b) harvesting the resultant recombinant, replication-defective adenovirus.

59. Purified recombinant, replication-defective adenovirus particles harvested in accordance with the method of claim 58.

60. A composition comprising purified recombinant adenovirus particles in
20 accordance with claim 59.

61. A composition in accordance with claim 60 which comprises a physiologically acceptable carrier.

62. A recombinant adenoviral vector in accordance with claim 56 which is at least partially deleted in E1 and devoid of E1 activity and comprises a heterologous nucleic acid.

63. A composition comprising purified recombinant adenoviral particles in accordance with claim 59 which are at least partially deleted in E1 and devoid of E1 activity and comprise a heterologous nucleic acid.

64. A method for effecting the delivery and expression of heterologous nucleic acid comprising administering the composition of claim 63 prior or subsequent to administration of the heterologous nucleic acid with the same or different vector.

65. A method in accordance with claim 64 wherein the composition is preceded or followed by administration of heterologous nucleic acid with an adenovirus of a different serotype.

66. A composition in accordance with claim 63 wherein the heterologous nucleic acid encodes an HIV antigen.

67. A method for generating a cellular-mediated immune response against HIV in an individual comprising administering to the individual a composition of claim 66.

68. A composition in accordance with claim 67 wherein the HIV antigen is HIV-1 gag or immunologically relevant modification thereof.

69. A composition in accordance with claim 67 wherein the HIV antigen is HIV-1 nef or immunologically relevant modification thereof.

70. A composition in accordance with claim 67 wherein the HIV antigen is HIV-1 pol or immunologically relevant modification thereof.

71. A recombinant adenoviral vector of serotype 34 which is at least partially deleted in E1 and devoid of E1 activity; wherein said vector comprises an E4 gene or a segment of an E4 gene from adenovirus serotype 5 comprising open reading frame 6 ("ORF6"), and a heterologous nucleic acid.

72. A population of cells comprising the recombinant adenoviral vector of claim 71.

73. A method for producing recombinant, replication-defective adenovirus particles comprising:

5 (a) introducing a recombinant adenoviral vector of claim 71 into a population of cells expressing adenovirus serotype 5 E1; and

(b) harvesting the resultant recombinant, replication-defective adenovirus.

74. Purified recombinant, replication-defective adenovirus particles harvested in accordance with the method of claim 73.

10 75. A composition comprising purified recombinant adenovirus particles in accordance with claim 74.

76. A composition in accordance with claim 75 which comprises a physiologically acceptable carrier.

15 77. A method for effecting the delivery and expression of the heterologous nucleic acid comprising administering the composition of claim 76 prior or subsequent to administration of the heterologous nucleic acid with the same or different vector.

78. A method in accordance with claim 77 above wherein the composition is preceded or followed by administration of the heterologous nucleic acid with an adenovirus of a different serotype.

20 79. A composition in accordance with claim 76 wherein the heterologous nucleic acid encodes an HIV antigen.

80. A method for generating a cellular-mediated immune response against HIV in an individual comprising administering to the individual a composition of claim 79.

81. A composition in accordance with claim 79 wherein the HIV antigen is HIV-1 gag or immunologically relevant modification thereof.

82. A composition in accordance with claim 79 wherein the HIV antigen is HIV-1 nef or immunologically relevant modification thereof.

5 83. A composition in accordance with claim 79 wherein the HIV antigen is HIV-1 pol or immunologically relevant modification thereof.